May 12, 2004

Via fax and UPS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2004N-0133
Electronic Record; Electronic Signatures; Public Meeting
[Federal Register Volume 69, No. 68, page 18591-18593, April 8, 2004.]

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. appreciates the opportunity to comment on the issues of the above-referenced Electronic Record; Electronic Signature Public Meeting.

We offer the following comments for your consideration.

IV.A.1: *"Should Part 11 be revised to implement the narrow interpretation described in the guidance?"*

Recommendation: Yes. We suggest that part 11 be revised to implement the narrow interpretation described in the guidance.

IV.A.2: *"We are interested in comments on whether revisions to definitions in part 11 would help clarify a narrow approach and suggestions for any revision."*

Recommendation: We suggest reviewing the regulation versus the guidance and place key changes into the regulation. We also suggest inserting into sections of the regulation, the concepts described in the guidance.

IV.A.3: *"...We are interested in comments on the need for clarification in part 11 regarding which records are required by predicate rules and are therefore required to be part 11 compliant."*

Recommendation: We suggest including a statement of predicate rule and providing a high-level, specific example in the guidance.

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IV.B.1: *"...We are interested in comments on whether there are other areas of part 11 that should incorporate the concept of a risk-based approach, detailed in the part 11 guidance (e.g., those that require operational system and device checks)."*

Recommendation: We suggest that FDA should not limit the use of Risk Based Approach (RBA). Organizations should be allowed to apply their risk-based approach to any area of part ll.

IV.B.2: *"Is additional clarity needed regarding how predicate rule requirements related to subpart B can be fulfilled?"*

Recommendation: We suggest that a statement should be included that describes what process to follow in the event that a predicate rule is silent on record management (e.g., when audit trail, retention, back-up, etc. needs to be present in Systems/Records and performed electronically).

IV.B.3: *"...Should the requirements for electronic records submitted to FDA be separate from electronic records maintained to satisfy predicate rule requirements?"*

Recommendation: No. We suggest that RBA should be used here as well and that appropriate integrity is required.

IV.B.4: *"...Should part 11 continue to differentiate between open systems and closed systems? ..."*

Recommendation: No. We suggest that a statement could be added in the e-record section with respect to additional controls for the system where the company does not control the access to the e-record and that RBA should be used to determine the nature and extent of controls.

IV.B.4.1: *"...Should we retain the validation provision under § 11.10(b) required to ensure that a system meets predicate rule requirements for validation?"*

Recommendation: Yes, we suggest that not all predicate regulations have specific requirements for validation systems of handling e-records.

IV.B.4.2: *"...Are there any related predicate rule requirements that you believe are necessary to preserve the content and meaning of records with respect to record copying and record retention? What requirements would preserve record security and integrity and ensure that records are suitable for inspection, review, and copying record retention?"*

Recommendation: In order to provide meaningful comments, clarification of the following question is needed: "*Are there any related predicate rule requirements that you believe are necessary to preserve the content and meaning of records with respect to record copying and record retention?"*

In addition, regarding the question: *What requirements would preserve record security and integrity and ensure that records are suitable for inspection, review, and copying record retention?"*, we prefer no specific elements in the regulation. However, we suggest that an RBA should be used to determine the extent of controls that are necessary for preserving content and meaning. We also suggest adding language regarding content and meaning in the regulations, and how it should be based on RBA.

IV.B.4.3: *"Should audit trail requirements include safeguards designed and implemented to deter, prevent, and document unauthorized record creation, modification, and deletion?"*

Recommendation: No, this is too specific. We suggest reliably determining the sequence of events that impacts record integrity, authenticity, and reliability. This should be based on RBA.

IV.B.4.4: *"...In light of how technology has developed since part 11 became effective, should part 11 be modified to incorporate concepts, such as configuration and document management, for all of a system's software and hardware?"*

Recommendation: No, the current wording is fine as is. Controls must be appropriate for the documentation and risk it introduces to the reliability of the system.

IV.C: *"...Should part 11 address investigations and follow-up when these security breaches occur?"*

Recommendation: Yes, we suggest that this is particularly important for e-signatures. We suggest focusing on ensuring that the signature is authentic and reliable. In addition, we suggest that a security investigation follow-up should be RBA based. Controls are necessary and are fine as stated.

IV.D.1: *"What are the economic ramifications of modifying part 11 based on the issues raised in this document?"*

Recommendation: We suggest that economic ramifications depend on the nature of the revision to part 11. If revisions become more prescriptive, there could be a large economic impact. If revisions are more general, neutral or cost savings could potentially be achieved.

IV.D.2: *"Is there a need to clarify in part 11 which records are required by predicate rules where those records are not specifically identified in predicate rules? If so, how could this distinction be made?"*

Recommendation: Yes, we suggest that if predicate rule is silent, then a positive change would be to indicate the direction to be taken. (e.g., user access files are not predicate rule requirements, however they show a that an individual was authorized at a given point in

time. Do we consider these as in or out of scope for part 11 required controls and are they technical and/or procedural?).

IV.D.3: *"In what ways can part 11 discourage innovation?"*

Recommendation: We suggest that part 11 adds more controls and prescriptive requirements that offer little or no value in assuring compliance beyond what is necessary.

IV.D.4: *"What potential changes to part 11 would encourage innovation and technical advances consistent with the agency's need to safeguard public health?"*

Recommendation: We suggest that Process Analytical Technology implementation is hindered due to concerns that data volumes cause retention, archival and retrieval to be expensive and burdensome. We also suggest that summary values are often needed to demonstrate commitment to required specifications, yet all data are or can be considered original observations by some inspectors.

IV.D.5: *What risk-based approaches would help to ensure that electronic records have the appropriate levels of integrity and authenticity elements and that electronic signatures are legally binding and authentic?"*

Recommendation: If this question refers to methods, then we suggest that FMEA would be an effective tool. If the question relates to process or methodology, then we suggest that the level of detail is too low. Further, we suggest that a regulation should indicate what, not how, to allow the widest possible use of tools.

IV.D.6: *"...What are the stakeholder concerns in regards to modifications make to legacy systems in use as of August 1997? Can the use of risk mitigation and appropriate controls eliminate concerns regarding legacy systems?"*

Recommendation: We suggest keeping the discussion in the guidance. We believe that the use of risk mitigation and appropriate controls is the correct approach to eliminate concerns regarding legacy systems.

IV.D.7: *"Should part 11 address record conversion?"*

Recommendation: Yes, we suggest that part 11 address record conversion for record availability and integrity in order to meet predicate rule requirements. We suggest that necessary controls should be determined using RBA.

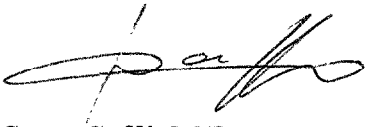
IV.D.8: *"Are there provisions of part 11 that should be augmented, modified, or deleted as a result of new technologies that have become available since part 11 was issued?"*

Recommendation: No, we suggest that a regulation based on fundamentals is key and changes in technology should not be a cause for revision. We suggest focusing on the

fundamentals and allow technology to support this. We also suggest that the RBA should be the mechanism to handle technology related evolutions.

On behalf of Aventis Pharmaceuticals Inc., we greatly appreciate the opportunity to comment on *Docket No. 2003N-0084 - Electronic Record; Electronic Signatures; Public Meeting* and are much obliged for your consideration.

Sincerely,



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